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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/331,808	01/27/2000	BJORN H. LINDQVIST	100084.410	2109

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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 07/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/331,808	LINDQVIST ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21,22,24-29,34-36,39 and 40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21,22,24-29,34-36,39 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Prosecution on the merits of this application is reopened in view of the new grounds of rejection and new found art as follows:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-22, 24-29, 34-36 and 39-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an ***in vitro*** method of P2A peptide and host cell, T7 S30 (E.Coli), does not reasonably provide enablement for an ***in vivo*** method using any type of organism using any cis-acting DNA binding protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include:

(1) the breadth of the claims,
(2) the nature of the invention,
(3) the state of the prior art,
(4) the level of one of ordinary skill;
(5) the level of predictability in the art,
(6) the amount of direction provided by the inventor,
(7) the existence of working examples, and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.
In re Wands, (U.S.P.Q. 2d 1400 (CAFC 1988).

1). The specification fails to give adequate direction and guidance for the claimed method of producing a peptide or protein expression library of any cis-acting DNA binding protein ***in vivo***. It does not teach how a skilled artisan can readily go about determining which organism expresses a cis-acting DNA protein or peptide library. It does not describe the kind, type, length of peptide or protein of a cis-acting DNA binding protein or kind of library expressed by any organism.

2). The specification failed to provide working examples for any of the numerous and different type of ***in vivo*** techniques using any type of organism for any type of cis-acting DNA protein in the instant method. As a skilled artisan knows expression of peptide in eukaryotic requires different conditions from those of prokaryotic organism. This is the more true since some of the microorganisms have complex sequences in the mega base pair. It is not apparent from the in vitro peptide library its extrapolation to the in vivo technique using a broad scope of

organisms. The specification is replete with general statements as to the vivo method. However, the exemplification is nil.

3). The breadth of the claims encompasses a large diversity of organism and the cis-acting DNA binding protein expressed by an organism. As a skilled artisan knows expression of peptide in eukaryotic requires different conditions from those of prokaryotic organism. The diversity of the inserts is not easily estimated from one organism to another. It may be for example, that only a small subset of possible peptide cis-acting DNA sequences is presented efficiently by a particular expression system of an organism. And, it is not always easy to follow the expression of peptides(not protein) in particular cells, let alone on any organism, for example, to know whether or not a specific cell or organism is expressing a member of the insert, especially for biological methods.

4). The state of the prior art is such that techniques as specifically applied for an in vitro method has been extrapolated to in vivo using broad expression organism. As a skilled artisan knows expression of peptide in eukaryotic requires different conditions from those of prokaryotic organism.

5). The art is inherently unpredictable because it is not possible to predict the organism that expresses a cis-acting DNA protein or peptide. This unpredictability is evident from the disclosure, page 9, last paragraph which states "..the process which allows the cis-protein to exhibit cis-action despite the presence of other appropriate binding sites on other DNA molecules also contained with the cell or organism is not known…." Furthermore, at page 11, first paragraph the specification recites that "….this [***in vitro***] radically reduces the time and effort involved in generating and screening and many of the ***limitations in vivo libraries are avoided***……..in vitro translation allows the incorporation of …..modifications …….some of which were not previously possible when translation was performed ***in vivo***" (Emphasis added). See also Masai et al (e.g., at paragraph bridging pages 6493-6494.)

6). Because the art is unpredictable, applicants' specification reasonably would not have assured persons skilled in the art that any (unnamed) organism expressing cis-acting DNA peptide or protein would result in the expression of a desired library with the DNA encoding sequence specifically bound to its protein by covalent binding. Applicants do not adequately enable persons skilled in the art to readily determine such. Applicants need not guarantee the success of the full scope of the claimed

invention. However, skilled artisans are provided with little assurance of success. [Reciting in vitro method employing S30 transcription/translation would obviate this rejection.]

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 21-22, 24-29, 34-36 and 39-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schatz(5498530) In view of Derbyshire (Molecular Microbiology) or Liu((Virology).

Schatz discloses in the Examples and figures a method of generating the peptide library comprises the steps of (a) constructing a recombinant DNA vector that encodes a DNA binding protein and contains binding sites for the DNA binding protein; (b) inserting into the coding sequence of the DNA binding protein in a multiplicity of vectors of step (a) coding sequences for random peptides such that the resulting vectors encode different fusion proteins, each of which is composed of the DNA binding protein and a random peptide; (c) transforming host cells with the vectors of

step (b); and (d) culturing the host cells transformed in step (c) under conditions suitable for expression of the fusion proteins. The peptide library produced by this method is especially useful in screening for ligands that bind to a receptor of interest. This screening method comprises the steps of (a) lysing the cells transformed with the peptide library under conditions such that the fusion protein remains bound to the vector that encodes the fusion protein; (b) contacting the fusion proteins of the peptide library with a receptor under conditions conducive to specific peptide-receptor binding; and (c) isolating the vector that encodes a peptide that binds to said receptor. By repetition of the affinity selection process one or more times, the vectors that encode the peptides of interest may be enriched. The recombinant vectors of the random peptide library are constructed so that the random peptide is expressed as a fusion product; the peptide is fused to a DNA binding protein. A DNA binding protein must exhibit high avidity binding to DNA and have a region that can accept insertions of amino acids without interfering with the DNA binding activity. Suitable DNA binding proteins include proteins selected from a large group of known DNA binding proteins including transcriptional regulators and proteins that serve structural functions on DNA. Examples include: proteins that recognize DNA

by virtue of a helix-turn-helix motif, such as the phage 434 repressor, the lambda phage cI and cro repressors, and the E. coli CAP protein from bacteria and proteins from eukaryotic cells that contain a homeobox helix-turn-helix motif; proteins containing the helix-loop-helix structure, such as myc and related; the phage P22 Arc and Mnt repressors (see Knight et al., 1989, J. Biol. Chem. 264(7):3639-3642 and Bowie and Sauer, 1989, J. Biol. Chem. 264.(13):7596-7602, each of which is incorporated herein by reference); and others. Schatz does not disclose that the DNA-binding protein is cis-proteins. However, Derbyshire et al discloses at page 1261 that cis proteins can work up to 1000-fold more efficiently if its gene is located close to is binding site. Liu disclose at page 163 that P2A is the best-studied system where A protein nicks the origin site and forms a covalent link to the cleaved strand. Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to employ cis- protein as the DNA-binding protein in the method of Schatz as taught by Liu or Derbyshire. The advantages in the use of said cis-protein as taught by Liu or Derbyshire would provide the motivation to one having ordinary skill in the art to make the modification at the time the invention was made.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571)272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571)272-4517. The fax phone number for the organization where this application or proceeding is assigned is(571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

Tdw

June 26, 2006